UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/814,826	03/31/2004	Pamela J. Fereira	3139-6351.1US (ALZ5019/32	5280

24247 7590 01/25/2008

TRASK BRITT
P.O. BOX 2550
SALT LAKE CITY, UT 84110

EXAMINER	
FRAZIER, BARBARA S	
ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
01/25/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPTOMail@traskbritt.com

Office Action Summary	Application No.	Applicant(s)	
	10/814,826	FEREIRA ET AL.	
	Examiner	Art Unit	
	BARBARA FRAZIER	4173	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *9,14 and 18-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10-13 and 15-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/31/04,5/13/05,5/15/06,6/29/06,8/21/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-17 in the reply filed on 12/28/07 is acknowledged. The traversal is on the ground(s) that the search and examination of all the claims in the application can be made without serious burden and the examiner can examine the claims on the merits. This is not found persuasive because, as stated previously in the Restriction Requirement filed 6/28/07, there would be a serious burden on the examiner if restriction is not required because the inventions have acquired a separate status in the art due to their recognized divergent subject matter. Specifically, there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

(a) the inventions have acquired a separate status in the art in view of their different classification;

(b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;

(c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);

(d) the prior art applicable to one invention would not likely be applicable to another invention;

(e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 18-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/28/07.

3. Applicant's election with traverse of the species drawn to omega-interferon (drug), benzyl alcohol (solvent), and polyvinylpyrrolidone (polymer), such as, for example, that described in Formulation A of Example 6 of the specification, in the reply filed on 12/28/07 is acknowledged. The traversal is on the ground(s) that the office has not demonstrated that the reasons it provides of independence and/or distinctness are actually supportive of that finding. This is not found persuasive because the Office action filed 6/28/07 states the election requirement and the reasons which support that finding, namely, that different combinations of chemicals will have different results, and the hundreds of combinations listed in the specification will result in different bioavailability, efficiency of drug delivery, and solubility of desired drug to be delivered. Additionally, Applicants traversal is on the grounds that restriction from all species claimed to just one species is not allowing applicant to claim a reasonable number of species as is provided for in the MPEP 806.04, and 37 CFR 1.141 provides that an allowable generic claim may link a reasonable number of species embraced thereby. This is not found persuasive because, as stated in the Office action filed 6/28/07, upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

The requirement is still deemed proper and is therefore made FINAL.

4. Claims 9 and 14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/28/07.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1-8, 10-13, and 15-17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 30-37 of copending Application No. 11/183,477. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to the same subject matter and composition components. Claim 30 of the '477 application is drawn to a stable non-aqueous drug formulation comprising a biocompatible polymer, a solvent, methionine, and a drug (compare instant claim 1). Claim 31 of the '477 application recites that the polymer is selected

from the group comprising polyvinylpyrrolidone (compare instant claims 8 and 15). Claims 32 and 33 of the '477 application recite that less than about 35% of the drug is degraded by chemical pathways, and less than about 15% of the drug is degraded through aggregation (compare instant claims 2 and 3). Claim 34 of the '477 application is drawn to the drug formulation comprising particulate material (compare instant claim 4). Claims 35-37 of the '477 application are drawn to the drug formulation comprising medicines including the protein interferon (compare instant claims 5-7). Using the specification of the '477 application as a dictionary, the specification further defines the drug formulation as being single-phase (Title; compare instant claim 1), miscible in water (paragraph 30; compare instant claim 1), having a viscosity in the range of about 1,000 to about 250,000 poise (paragraph 45; compare instant claim 10), comprising about 40% to about 80% polymer and about 20% to about 60% solvent (paragraph 46; compare instant claim 11), wherein the vehicle exhibits a moisture content of less than 5% (paragraph 49; compare instant claim 13), wherein the vehicle exhibits peroxide values below 5 ppm (paragraph 32; compare instant claim 16), and wherein the biomolecular material (drug) is dispersed within the vehicle as a dry particulate material to create a suspension (paragraph 51; compare instant claims 12 and 17). Additionally, the formulation is defined as comprising omega interferon (paragraph 79), polyvinylpyrrolidone (claim 31), and benzyl alcohol (paragraph 44; compare claim 15 and the elected species).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8, 10-13, and 15-17 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses formulations, such as Formulation A and Formulation B, which consist of 40% BA, 60% PVP, omega-interferon particles that consist of 7 parts citrate for every 4 parts omega-interferon, with a particle loading of 9.6% (wt/wt) for Formulation A and a particle loading of 3.8% (wt/wt) for Formulation B, and with each formulation having a moisture level of less than 3% and peroxide level less than 5 ppm, which meet the written description and enablement provisions of 35 USC 112, first paragraph. However, claims 1-8, 10-13, and 15-17 are directed to encompass formulations wherein the elected specie components (i.e., omega-interferon, benzyl alcohol, and polyvinylpyrrolidone) are present in different amounts, and having other moisture and peroxide levels, and having drug particles with other additives, which only correspond in some undefined way to specifically instantly disclosed formulations. None of these formulations meet the written description provision of 35 USC § 112, first paragraph, due to lacking the property information for what they are and such formulations are highly variant and encompass a myriad of possibilities, such that it cannot be determined which particular combinations of component amounts, particle additives, and moisture and peroxide levels will

result in the properties of being 1) stable, 2) nonaqueous, 3) single-phase, 4) miscible with water, 5) wherein the drug is insoluble in one or more vehicle components, and 6) wherein the drug formulation is stable at 37 degrees C for at least two months, all of which properties are required by independent claim 1. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of the above specifically disclosed formulations, the skilled artisan cannot envision the detailed combinations of other formulations, regardless of the complexity or simplicity of the method of formation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for making it. The formulation itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only the above defined formulations, but not the full breadth of the claim(s) meet the written description provision of 35 USC § 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC § 112 is severable from its enablement provision. (See page 1115.)

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-8, 10-13, and 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berry et al., WO 00/45790, and Chen et al., US 2003/018036.

The claimed elected invention is drawn to a stable nonaqueous drug formulation comprising at least one drug comprising omega-interferon; and a nonaqueous, single-phase vehicle comprising at least one polymer comprising polyvinylpyrrolidone and at least one solvent comprising benzyl alcohol, the vehicle being miscible in water, wherein the drug is insoluble in one or more vehicle components and the drug formulation is stable at 37 degrees C for at least two months (see claim 1 and the elected species).

Berry et al. disclose stable non-aqueous single phase viscous vehicles and formulations comprising at least one beneficial agent uniformly suspended in the vehicle (abstract). The vehicle comprises polymer and solvent (page 6, lines 17-18) wherein the polymer is about 5% to about 30% and the solvent is about 30% to about 50% of the vehicle (page 6, lines 20-22). The beneficial agent may be interferons (page 13, lines 29) and the polymer may be polyvinylpyrrolidone (page 12, line 18). The formulations may be stored at temperatures ranging from cold to body temperature (about 37 degrees C) for long periods of time (1 month to 1 year or more) (page 6, lines 27-30). Berry et al. differ from the claimed invention because benzyl alcohol is used as a preservative (page 11, line 22) instead of as a solvent, omega-interferon is not listed as one of the interferons used as the beneficial agent, and the formulation is not taught as being miscible in water. Chen et al. disclose catheter injectable depot compositions comprising polyvinylpyrrolidone polymer (paragraph 75) and benzyl alcohol solvent (paragraph 76); experimental data using the formulations made reveals that compositions comprising benzyl alcohol as the solvent show an improvement by reducing the injection force of the depot gel formulation (Examples 15 and 17). Chen et al. also teach that omega-interferon may be used as the beneficial agent (paragraph 178), and that the compositions comprising

polyvinylpyrrolidone and benzyl alcohol have a measure of miscibility in water (paragraph 21). Both the formulations of Berry et al. and the compositions of Chen et al. are drawn to compositions comprising interferon, polyvinylpyrrolidone, and solvent, to be used in drug delivery systems.

It is generally considered to be prima facie obvious to combine components each of which is taught by the prior art to be useful for the same purpose in order to form a composition that is to be used for an identical purpose. The motivation for combining them flows from their having been used individually in the prior art, and from the being recognized in the prior art as useful for the same purpose. As shown by the recited teachings, instant claims are no more than the combination of conventional components of compositions for drug delivery systems. It therefore follows that the instant claims define prima facie obvious subject matter. Cf. In re Kerkhoven, 626 F.2d 848, 205 USPQ 1069 (CCPA 1980).

Therefore, it would have been prima facie obvious at the time the invention was made to form a stable, nonaqueous composition by combining the interferon, polyvinylpyrrolidone and solvent of Berry et al. with the omega-interferon, polyvinylpyrrolidone and benzyl alcohol of Chen et al. in order to arrive at the claimed invention, with a reasonable expectation of success.

With respect to the drug being insoluble in one or more vehicle components (claim 1), Berry et al. teach that the beneficial agent is uniformly suspended in the vehicle (not solubilized), and thus would not be soluble in at least one of the vehicle components.

With respect to the amount and method of degradation of the drug (claims 2 and 3), Berry et al. does not specifically teach the percentage of drug degraded by chemical pathways or aggregation. However, Berry et al. do teach that the formulations maintain a high level of stability over time, wherein greater than 70% of the formulation is recovered at seven weeks (Tables 5 and 6). Based on this data, one skilled in the art would conclude that the level of degradation of the formulations would be comparable to that described in the claimed invention.

With respect to the drug being a particulate material (claim 4) that is dry (claim 12) and dispersed with the vehicle as a suspension (claim 17), Berry et al. teach that the active agent is buffered, then spray dried (page 16) before forming a uniform dispersion (page 17); Berry et al. also teach that drying the beneficial agent prior to formulation enhances the stability of the formulation (page 15).

With respect to the viscosity of the formulation (claim 10), Berry et al. describes the vehicle of the formulation as a "viscous vehicle", which means a viscosity the is preferably about 10,000 to 250,000 poise; this is encompassed by Applicant's viscosity of about 1,000 to about 250,000 poise.

With respect to the amounts of polymer and solvent (claim 11), Berry et al. disclose that the amount of the polymer is about 5% to about 30% and the amount of solvent is about 30% to about 50% of the vehicle (page 6, lines 20-22). This appears to be comparable to the amounts claimed by Applicants, especially given that the prior art uses the flexible modifier "about". In any case, it would have been obvious to determine workable and/or optimal amounts of polymer and solvent per the reasoning of well-established precedent, such as In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). (Holding that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.")

With respect to moisture content (claim 13), Berry et al. teach that the final moisture content of the viscous vehicle was less than 2% (page 15, line 2).

With respect to peroxide values (claim 16), Berry et al. do not specifically teach the peroxide values of the formulation. However, Berry et al. do teach that peroxides "not only

adversely affect protein stability but would be toxic when delivered directly to, for example, the central nervous system of a human or animal (page 4, lines 23-24). Therefore, one skilled in the art would assume that the peroxide values of the formulations made by Berry et al. and Chen et al. would also be less than 5 ppm, especially given the fact the components and use of the compositions of Berry et al. and Chen et al. and the compositions of the claimed invention are the same.

It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barbara Frazier whose telephone number is (571)270-3496. The examiner can normally be reached on Monday-Thursday 8am-4pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)272-0718, or Cecilia Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BSF

/Cecilia Tsang/
Supervisory Patent Examiner, Art Unit 4173